Data-driven multiscale model of primary motor cortex microcircuits (U01EB017695)

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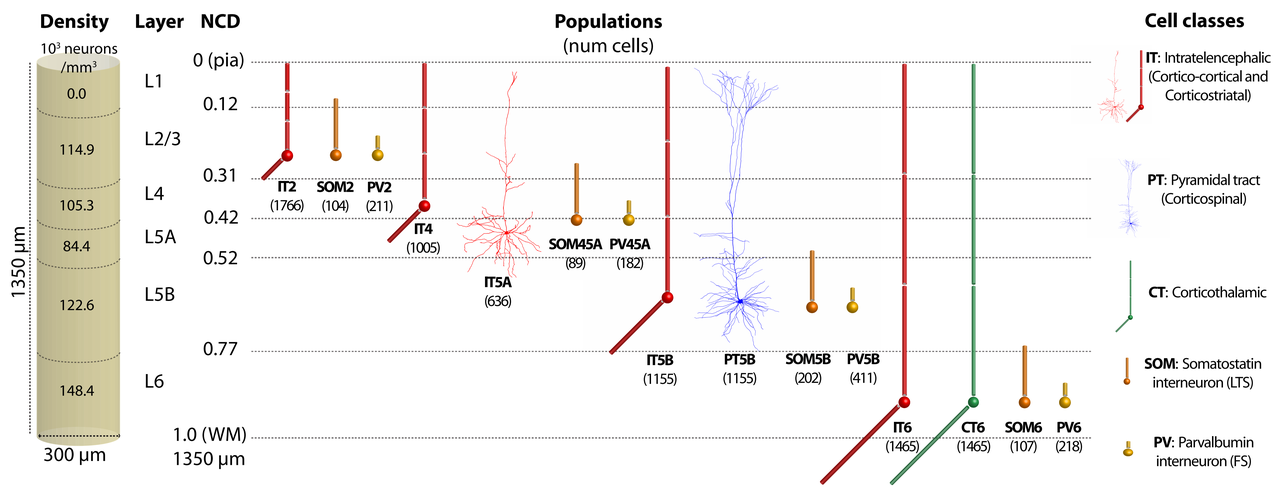
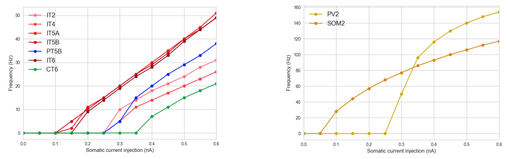
Cell populations

Mouse 6-layer M1 with **10,171 neurons** of 5 classes distributed in 15 populations
Full scale cylindric volume of **300 µm** (diameter) x **1350 µm** (cortical depth) with realistic cell densitites and ratios



Simplified 6 compartment and detailed 700+ compartment morphologies from 3D reconstructions.
Ionic channel distributions (Na, Kdr, Ka, Kd, HCN, CaL, CaN, KCa) constrained by literature and optimized to reproduce in vitro f-I curve and voltage shape.

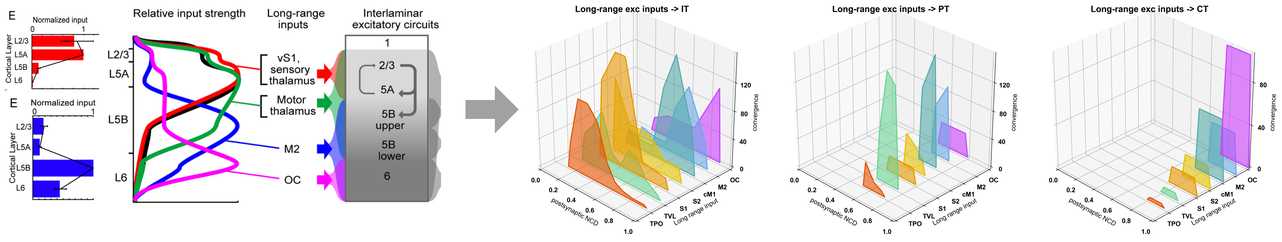
(Harrison & Shepherd 2015, Suter et al 2013, Anderson et al 2010, Yamawaki et al 2015, Tsai et al 2009, Lefort et al 2009, Neymotin et al 2016, Katzel et al 2011, Wall et al 2016, Oswald et al 2013, Konstantoudak et al 2013, Naka & Adesnik 2016)



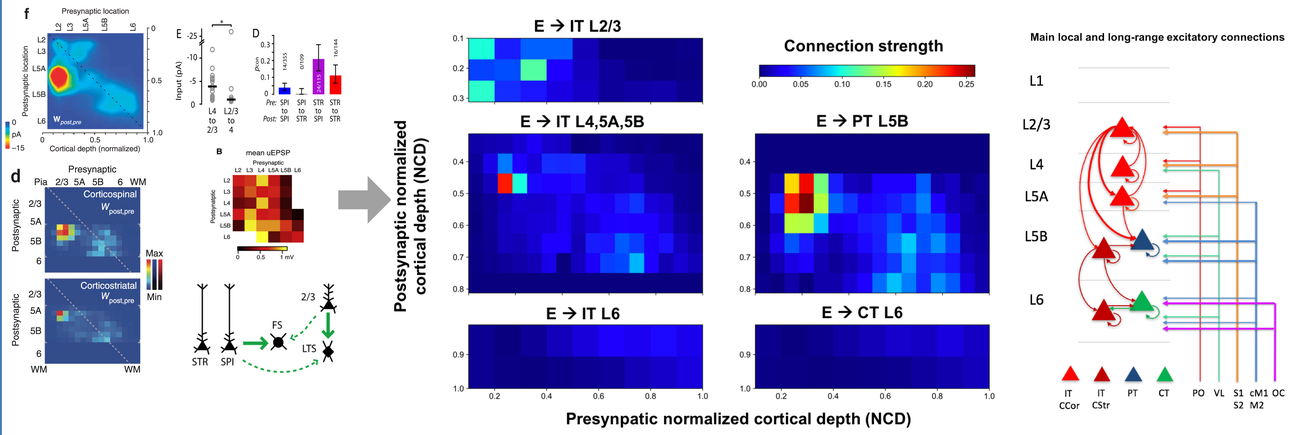
Connectivtiy

Combines connectivity data from several studies at **multiple scales (long-range, local, dendritic)** into unified model.
Connectivity at all scales as a function of pre- and post-synaptic **cell type** and normalized **cortical depth** (NCD).

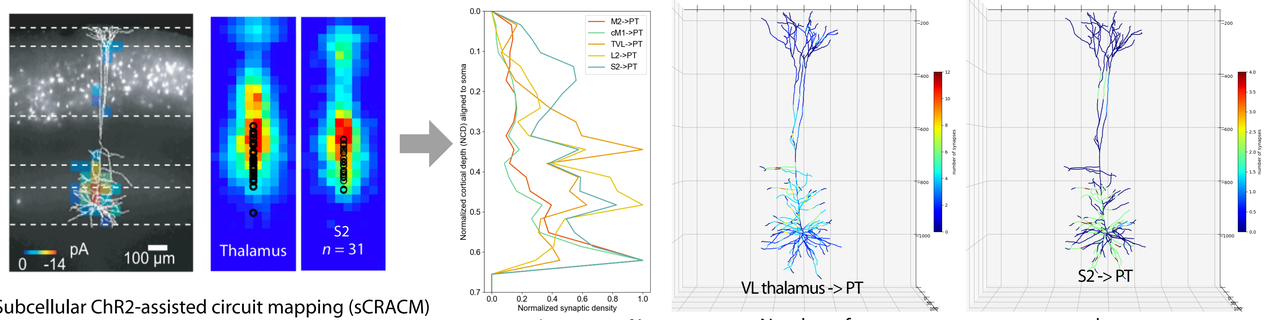
Long-range from other brain areas



Local M1 microcircuits



Dendritic distribution of synapses



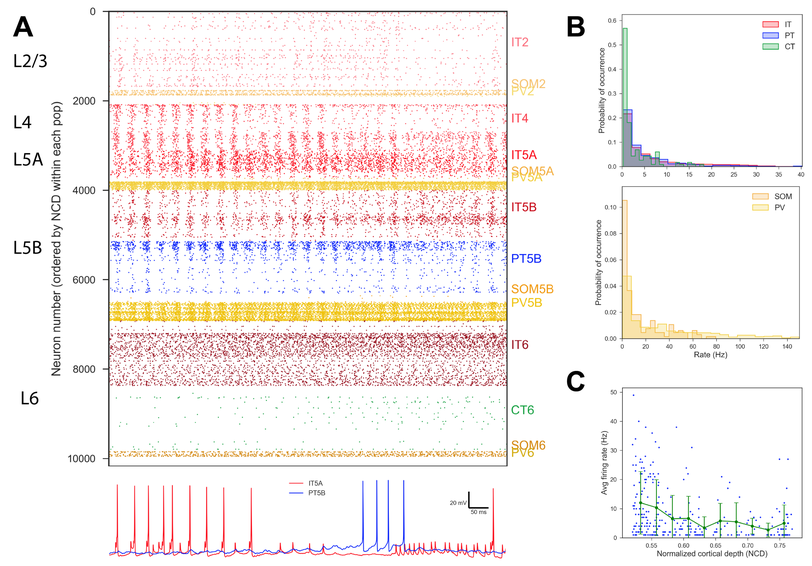
Subcellular ChR2-assisted circuit mapping (sCRACM)

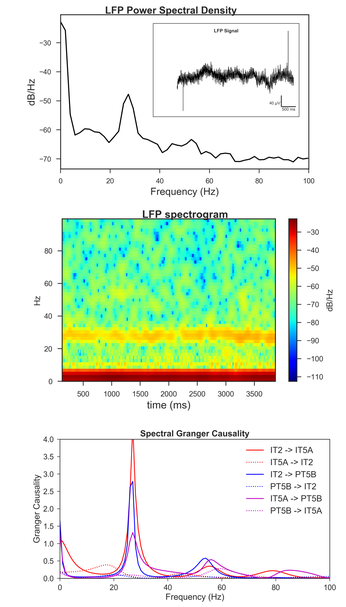
Synaptic density profile (dendritic density corrected)

Number of synapses per compartment shows complementary distribution of synaptic inputs from VL vs S2

(Weiler et al 2008, Anderson et al 2010, Suter et al 2015, Hooks et al 2013, Kiritani et al 2012, Lefort et al 2009, Apicella et al 2011, Yamawaki & Shepherd 2015, Yamawaki et al 2015, Naka & Adesnik 2016, Katzel et al 2011, Fino & Yuste 2011, Mao et al 2011)

Spontaneous activity (driven by long-range inputs)

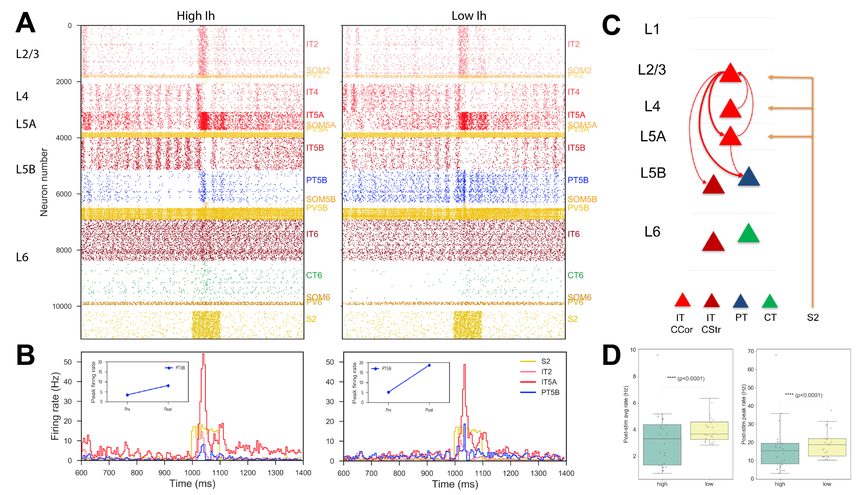




- Spontaneous firing rates exhibit distributions and spatial properties that match cortical data.
- Neural activity depends on cell class, cortical layer and sublaminar location, e.g. PT activity within layer 5B decreased with cortical depth.

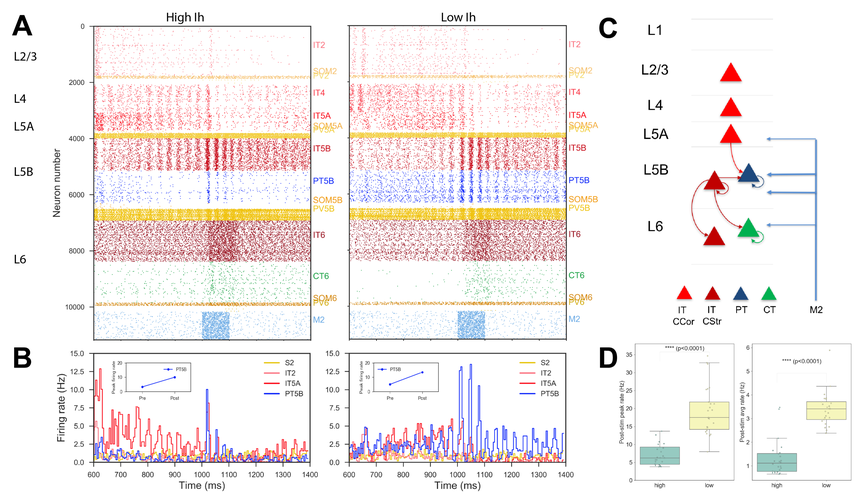
- LFP oscillations in the beta and gamma range emerged in the absence of rhythmic external inputs.
- Information flowed from IT->PT but not opposite direction (peak in beta).

Response to pulse from S2 (sensory-related input)



- Pathway: sensory-related inputs --> upper IT --> PT
- Sensory input + high Ih = high IT and low PT
- Sensory input + low Ih = high IT and high PT
- Statistically significant effect of Ih (N=5 wiring x 5 input seeds)
- Downregulation of Ih facilitates synaptic integration of inputs and increased PT output activity.
- Potential mechanism to switch between motor planning and execution

Response to pulse from M2 (motor-related input)



- Pathway: motor-related inputs --> PT (directly)
- Motor input + high Ih = low IT and low PT
- Motor input + low Ih = low IT and high PT
- Statistically significant effect of Ih (N=5 wiring x 5 input seeds)
- Additional simulations (not shown) look at 1) interaction between S2 and M2 inputs as function of interval between them; 2) information flow of long time-varying inputs recorded from mouse S2; 3) network resonance in response to L2/3 inputs at different frquencies.

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